

## CLAIMS

1. A composition for preparing a stimuli responsive hybrid hydrogel comprising a polymeric network consisting essentially of a water soluble polymer crosslinked by a protein domain.

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2. A composition according to Claim 1 wherein the crosslinking of the protein domain to the polymer is by means of non-covalent bonding selected from the group consisting of chelation bonding, coordination bonding, biotin-<sup>avidin</sup>~~avidin~~ bonding, protein-protein interaction and protein-ligand interaction.

3. A composition according to Claim 2 wherein the crosslinking of the protein domain to the polymer is by means of chelation bonding.

4. A composition according to Claim 2 wherein the crosslinking of the protein domain to the polymer is by means of biotin-<sup>avidin</sup>~~avidin~~ bonding.

5. A composition according to Claim 2 wherein the crosslinking of the protein domain to the polymer is by means of protein-protein interaction.

5 6. A composition according to Claim 2 wherein the crosslinking of the protein domain to the polymer is by means of protein-ligand interaction.

7. A composition according to Claim 1 wherein the crosslinking of the protein domain to the polymer is by means of covalent or coordination bonding.

8. A composition according to either Claims 2 or 7 wherein the protein domain has a coiled-coil structure.

9. A composition according to either Claims 2 or 7 wherein the protein domain is a recombinant protein domain.

10. A composition according to either Claims 2 or 7 wherein the water soluble polymer is a member selected from the group consisting of copolymers of N-substituted methacrylamides,

copolymers of N, N-disubstituted acrylamides, hydrophilic esters of methacrylic or acrylic acid, N-vinylpyrrolidone, N-acryloylmorpholine, sulfoethylmethacrylate, acrylic and methacrylic acid, di-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO), and tri-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO) and the derivatives thereof.

11. A composition according to Claim 10 wherein the water soluble polymer is <sup>a copolymer of</sup> ~~an~~ N-substituted methacrylamide and the derivatives thereof.

12. A composition according to Claim 11 wherein the N-substituted methacrylamide is a member selected from the group consisting of N-(2-hydroxypropyl)methacrylamide (HPMA), copolymers of N-(N',N'-dicarboxymethylaminopropyl) methacrylamide (DAMA), and copolymers of HPMA and N-(3-aminopropyl)methacrylamide and the derivatives thereof.

13. A composition according to Claim 10 wherein the water soluble polymer is a member selected from the group consisting of di-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO), tri-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO) and the derivatives thereof.

14. A composition according to Claim 10 wherein the water soluble polymer is copolymer of a member selected from the group consisting of ~~N-disubstituted~~ <sup>N-disubstituted</sup> acrylamides, hydrophilic esters of methacrylic or acrylic acid, N-vinylpyrrolidone, N-acryloylmorpholine, sulfoethylmethacrylate, acrylic and methacrylic acid and the derivatives thereof.

15. A composition according to either Claim 2 or 7 wherein the molar ratio of the water soluble polymer to the crosslinking protein domain is within a range of about 1:1 and 1:500.

16. A composition according to Claim 15 wherein the molar ratio of the water soluble polymer to the crosslinking protein domain is within a range of about 1:1 to 1:300.

17. A composition according to either 2 or 7 further comprising a bioactive agent.

18. A composition according to 17 wherein the bioactive agent is an oligo- or poly-peptide.

19. A composition according to 18 wherein the peptide is conjugated with the crosslinking protein domain.

20. A composition according to 17 wherein the bioactive agent is DNA or RNA.

21. A stimuli responsive hydrogel comprising the composition of claim 1 in a three dimensional aqueous solution <sup>swollen</sup> ~~swelled~~ state.

22. A stimuli responsive hydrogel according to Claim 21 wherein the crosslinking of the protein domain to the polymer is by means of non-covalent bonding selected from the group consisting of chelation bonding, coordination bonding, biotin-<sup>avidin</sup> ~~avidin~~ bonding, protein-protein interaction and protein-ligand interaction.

23. A stimuli responsive hydrogel according to Claim 22 wherein the crosslinking of the protein domain to the polymer is by means of chelation bonding.

5 24. A stimuli responsive hydrogel according to Claim 22 wherein the crosslinking of the protein domain to the polymer is by means of biotin-<sup>avidin</sup>~~avidin~~ bonding.

25. A stimuli responsive hydrogel according to Claim 22 wherein the crosslinking of the protein domain to the polymer is by means of protein-protein interaction.

26. A stimuli responsive hydrogel according to Claim 22 wherein the crosslinking of the protein domain to the polymer is by means of protein-ligand interaction.

27. A stimuli responsive hydrogel according to Claim 21 wherein the crosslinking of the protein domain to the polymer is by means of covalent or coordination bonding.

28. A stimuli responsive hydrogel according to either Claims 21 or 27 wherein the protein domain has a coiled-coil structure.

29. A stimuli responsive hydrogel according to either Claims 21 or 27 wherein the protein domain is a recombinant protein domain.

30. A stimuli responsive hydrogel according to either Claims 21 or 27 wherein the water soluble polymer is a member selected from the group consisting of copolymers of N-substituted methacrylamides, copolymers of N, <sup>N-disubstituted</sup> ~~N-disubstituted~~ acrylamides, hydrophilic esters of methacrylic or acrylic acid, N-vinylpyrrolidone, N-acryloylmorpholine, sulfoethylmethacrylate, acrylic and methacrylic acid, di-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO), and tri-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO) and the derivatives thereof.

31. A stimuli responsive hydrogel according to Claim 30 wherein the water soluble polymer is <sup>a Copolymer of</sup> ~~an~~ N-substituted methacrylamide and the derivatives thereof.

32. A stimuli responsive hydrogel according to Claim 31 wherein the N-substituted methacrylamide is a member selected from the group consisting of N-(2-hydroxypropyl)methacrylamide (HPMA), copolymers of N-(N',N'-dicarboxymethylaminopropyl) methacrylamide (DAMA), and copolymers of HPMA and N-(3-aminopropyl)methacrylamide and the derivatives thereof.

33. A stimuli responsive hydrogel according to Claim 30 wherein the water soluble polymer is a member selected from the group consisting of di-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO), tri-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO) and the derivatives thereof.

34. A stimuli responsive hydrogel according to Claim 30 wherein the water soluble polymer is copolymer of a member selected from the group consisting of ~~N-disubstituted~~ <sup>N-disubstituted</sup> acrylamides, hydrophilic esters of methacrylic or acrylic acid, N-vinylpyrrolidone, N-acryloylmorpholine, sulfoethylmethacrylate, acrylic and methacrylic acid and the derivatives thereof.



35. A stimuli responsive hydrogel according to either Claim 21 or 27 wherein the molar ratio of the water soluble polymer to the crosslinking protein domain is within a range of about 1:1 and 1:500.

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36. A stimuli responsive hydrogel according to Claim 35 wherein the molar ratio of the water soluble polymer to the crosslinking protein domain is within a range of about 1:1 and 1:300.

10 37. A stimuli responsive hydrogel according to either 21 or 27 further comprising a bioactive agent.

15 38. A stimuli responsive hydrogel according to 37 wherein the bioactive agent is a oligo- or poly- peptide.

20 39. A stimuli responsive hydrogel according to 38 wherein the peptide is conjugated the crosslinking protein domain.

40. A stimuli responsive hydrogel according to 37 wherein the bioactive agent is DNA or RNA molecule.

41. A stimuli responsive hydrogel according to 37 wherein the bioactive agent is <sup>soluble</sup>~~insoluble~~ in the aqueous solution.

42. A stimuli responsive hydrogel according to either Claims 21  
5 or 27 wherein the aqueous solution in equilibrium swollen state is with a range of between 1 to 99% (w/w).

43. A stimuli responsive hydrogel according to either Claims 42  
10 or 27 wherein the aqueous solution in equilibrium swollen state is with a range of between 5 to 99% (w/w).

44. A stimuli responsive hydrogel according to either Claims 43  
15 or 27 wherein the aqueous solution in equilibrium swollen state is with a range of between 10 to 99% (w/w).